App. No. 10/521,234
Office Action Dated December 16, 2008

REMARKS

Favorable reconsideration is respectfully requested in view of the above amendments and following remarks. Claims 11, 14 and 15 have been amended. Claims 11 and 14 have been amended editorially. The amendment to claim 15 is supported by the original disclosure, for example by original claims 8, 10, 12 and 13 and page 4, lines 22-37 and page 7, lines 3-6 and 8-15 of the specification. Claims 8, 10, 12 and 13 have been canceled without prejudice or disclaimer. No new matter has been added. Claims 11, 14 and 15 are pending.

Claim 11 is objected to because of informalities. Claim 11 has been amended, taking the issues noted in the objection into account.

Claims 8 and 10-15 have been rejected under 35 U.S.C. 112, second paragraph, as being indefinite. Claim 15 is directed to measuring an amount of glycated protein. Claim 15 recites that the redox reaction is measured by determining an amount of hydrogen peroxide generated by the reaction of the glycated portion of the glycated protein degradation product and the frucytosyl amino acid oxidase. Claim 15 further recites that the amount of the hydrogen peroxide is determined by using an oxidase to reduce the generated hydrogen peroxide and oxidize a substrate that develops color by oxidation and measuring a degree of the color that the substrate has developed. Applicants submit that claim 15 is definite.

Claims 11-15 are rejected under 35 USC 103(a) as being unpatentable over Komori et al. (EP 1002874) and Glossary of class names of organic compounds (PAC, 1995, 67, 1307, pages 1351-1396), in view of Benezra et al. (US Patent No. 5,468,640) and further in view of Ishimaru et al. (US Patent No. 6,127,138). Applicants respectfully traverse the rejection.

Komori et al. aim to eliminate the influence of any reducing substance contained in the sample and teaches that this can be accomplished by adding a tetrazolium compound prior to the redox reaction (paragraph [0010]). Komori et al. teach that the tetrazolium compound that accomplishes their objective is a compound having a tetrazole ring (Id.). The Glossary of class names of organic compounds merely defines a sulfonic acid compound and a nitro compound.

On the other hand, claim 15 requires treating a sample containing the glycated protein with a protease in the presence of a sulfonic acid compound and a nitro compound. Claim 15 further requires the sulfonic acid compound to be at least one selected from the group consisting of 4-aminoazobenzene-4'-sulfonic acid sodium salt, 4-amino-4'-nitrostilbene-2,2'-disulfonic acid disodium salt, 4,4'-diazidostilbene-2,2'-disulfonic acid disodium salt, N-cyclohexyl-2-aminoethane sulfonic acid, N-cyclohexyl-3-aminopropane sulfonic acid, N-cyclohexyl-2-hydroxy-3-aminopropane sulfonic acid, piperazine-1,4-bis(2-ethane sulfonic acid) and bathophenanthroline sulfonic acid. Claim 15 also requires the nitro compound to be at least one selected from the group consisting of 2,4-dinitrophenol, 2,5-dinitrophenyl, 2,6-dinitrophenyl, 4,6-dinitro-2-methyl phenol, 2-amino-4-nitrophenol, 2-amino-5-nitrophenol, 2-amino-4-nitrophenol, p-nitrophenol, 2,4-dinitroaniline, p-nitroaniline, 4-amino-4'-nitrostilbene-2, 2'-disulfonic acid disodium salt and nitrobenzene.

The sulfonic acid compounds required by claim 15 generally have a high solubility, such that they can be treated easily even when the concentration of glycated proteins in the sample is high (see page 4, lines 6-9). Moreover, when the protease treatment is conducted in the presence of one or more of the sulfonic acid compounds and one or more of the nitro compounds as required by claim 15, the degradation time is accelerated significantly, thereby allowing a high degradation efficiency. As a result, the accuracy of measurement is improved considerably (see page 16, lines 3-11 for example). Nothing in Komori et al. teaches or suggests using a compound other than a tetrazolium compound, let alone the use of the specific sulfonic acid compounds and the nitro compounds required by claim 15 or the accompanying benefits. Accordingly, claim 15 and the dependent claims therefrom are patentable over Komori et al.

The rejection relies on Benezra et al. for the use of lithium lauryl sulfate. The rejection's reliance is moot, as claim 15 does not require the use of lithium lauryl sulfate.

Ishimaru et al. do not cure the deficiencies of Komori et al. and Benezra et al. Although Ishimaru et al. disclose the use of metalloprotease, nothing in Ishimaru et al. teaches or suggests the use of the sulfonic acid compounds and the nitro compounds required by claim 15 during the protease treatment, nor any reason to expect that the

sulfonic acid compounds and the nitro compounds required by claim 15 could be used with a protease to achieve superior degradation of glycated protein.

Accordingly, for at least the above reasons, claim 15 is patentable over Komori et al., Benezra et al. and Ishimaru et al., taken alone or together. Claims 11 and 14 are also patentable over the references since they depend from claim 15 that is allowable. Reversal of the rejection is respectfully requested.

Claims 8, 10 and 15 are rejected under 35 USC 103(a) as being unpatentable over Komori et al. (EP 1002874) in view of Kaminagayoshi et al. (EP 0158964) and further in view of Armstrong (US Patent No. 4,102,810) and further in view of Johnson et al. (Blood, 1994, Vol. 83, No. 4, p. 1117-1123). The rejection is rendered moot, as claims 12 and 13, which were not included in the rejection, have been incorporated into claim 15.

Moreover, the rejection relies on Kaminagayoshi et al. for the use of dodecylbenzenesulfonic acid sodium salt and Armstrong for use of sodium nitrite. The rejection's reliance is moot, as claim 15 does not require the use of dodecylbenzenesulfonic acid sodium salt and sodium nitrite.

The rejection relies on Johnson et al. for the use of 2,4-dinitrophenyl. The rejection's reliance is misplaced. Johnson et al. is directed to studying chronic hemolysis found in $G6PD^{Wayne}$ by using 1-chloro-2,4-dinitrobenzene (CDNB) to lower GSH levels in normal red blood cells to determine the role of GSH in protecting membrane proteins against oxidation and maintaining membrane stability (page 1120, col. 2). Claim 15 does not require the use of 1-chloro-2,4-dinitrobenzene (CDNB). While Johnson et al. teach the formation of 2,4-dinitrophenyl-S-glutathione by the reaction of intraerythrocytic GSH with CDNB, there is no experimental work or detailed explanation that would lead one to expect with any reasonable degree of certainty that the use of CDNB would be appropriate with systems that measure the oxidation of glycated proteins. To the contrary, Johnson et al. note that when GSH was reduced to undetectable levels by addition of CDNB, there was extensive hemoglobin oxidation in the cells (page 1120, col. 2). Thus, one would question whether, after adding CDNB to Komori et al.'s system before the redox reaction with FAOD, the hydrogen peroxide generated from the glycated proteins that have been

extensively oxidized by the presence of CDNB would accurately reflect the actual amount of glycated protein.

As indicated above, nothing in Komori et al. teaches or suggests using a compound other than a tetrazolium compound, let alone the use of the specific sulfonic acid compounds and the nitro compounds required by claim 15. Kaminagayoshi et al., Armstrong and Johnson et al. do not cure the deficiencies of Komori et al. Accordingly, claim 15 and the dependent claims therefrom are patentable over the references taken alone or together.

In view of the above, favorable reconsideration in the form of a notice of allowance is requested. Any questions or concerns regarding this communication can be directed to the attorney-of-record, Douglas P. Mueller, Reg. No. 30,300, at (612) 455.3804.

Respectfully submitted,

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